PCT/FR2002/004587

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference CP.60/558PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/FR2002/004587	International filing date (*day/month/year*) 30 décembre 2002 (30.12.2002)	Priority date (*day/month/year*) 31 décembre 2001 (31.12.2001)
International Patent Classification (IPC) or national classification and IPC C12N 15/10, C12Q 1/68		
Applicant INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (I.N.S.E.R.M.)		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17 juin 2003 (17.06.2003)	05 February 2004 (05.02.2004)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR2002/004587

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

☒ the international application as originally filed.

☐ the description, pages 1-11, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☐ the claims, Nos. 1-12, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. _____, filed with the letter of _____,
Nos. _____, filed with the letter of _____.

☐ the drawings, sheets/fig 1-110, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRE[redacted]NARY EXAMINATION REPORT

Inte[redacted]nal application No.
PC[redacted]FR 02/04587

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2	YES
	Claims	1, 3	NO
Inventive step (IS)	Claims		YES
	Claims	1-3	NO
Industrial applicability (IA)	Claims	1-3	YES
	Claims		NO

2. Citations and explanations

1. Reference is made to the following documents:

D1: WO 98 17805 A (RAYMOND NIGEL; QUINN FREDERICK D (US); US HEALTH (US); RIBOT EFRAI) 30 April 1998 (1998-04-30)

D2: PELICIC V ET AL: 'Mutagenesis of Neisseria meningitidis by in vitro transposition of Himar1 mariner.' JOURNAL OF BACTERIOLOGY. UNITED STATES OCT 2000, vol. 182, no. 19, October 2000 (2000-10), pages 5391-5398, ISSN: 0021-9193 cited in the application

D3: NASSIF X ET AL: 'What do we know about the entry of Neisseria meningitidis into the meninges?' EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 95, no. 4, 12 October 1997 (1997-10-12) pages 219-235, ISSN: 0223-5234

2. NOVELTY (PCT Article 33(2))

2.1 D1 describes a method for detecting the genes of pathogenic bacteria, particularly *Neisseria meningitidis*, which express a desired phenotype (page 50, lines 30-31: "ability to attach or invade

human endometrial tissue culture (HEC-1-B) cells"), characterised in that use is made of a bank containing mutants obtained by transposition (page 50, lines 29-30; page 52, lines 24-26) that are contacted with an environment capable of interacting with the mutant bacteria expressing the desired phenotype (page 53, lines 1-2: contact with endothelial HEC-1-B cells), whereafter the bacteria that failed to interact with the desired phenotype are recovered (page 50, lines 32-33), the mutant genes in said bacteria are identified, and the involvement thereof in said phenotype is verified (page 51, lines 30-33; page 52, lines 21-23). Therefore, the subject matter of claims 1 and 3 of the present application is not novel over D1.

2.2 D2 describes a method for detecting the genes of pathogenic bacteria (*Neisseria meningitidis*) which express a desired phenotype (page 5395, column 1: "ability to utilize maltose"), characterised in that use is made of a bank containing mutants obtained by transposition (page 5394, "Transposition on chromosomal DNA: random mutagenesis") that are contacted with an environment capable of interacting with the mutant bacteria expressing the desired phenotype (page 5392, column 1, paragraph "Bacterial cultures", second indent), whereafter the bacteria that failed to interact with the desired phenotype are recovered (page 5395, column 1, "identification of 4 [...] clones [...] with an impaired capacity to produce acid during maltose catabolism"), the mutant genes in said bacteria are identified, and the involvement thereof in said phenotype is verified (page 5395, column 2, "In mal1, Himar1 was inserted within a gene encoding a putative respiratory D-

lactate dehydrogenase"). Therefore, the subject matter of claim 1 of the present application is not novel over D2.

3. INVENTIVE STEP (PCT Article 33(3))

3.1 D2 describes a method for detecting the genes of pathogenic bacteria, particularly *Neisseria meningitidis* (cf. point 2.1 above), from which the subject matter of claim 2 differs in that, during the contacting step, the mutants are transferred from the bank into serum.

3.2 The problem that the present invention is intended to solve can thus be considered to be that of providing a method for detecting the genes of pathogenic bacteria involved in the expression of an alternative phenotype.

3.3 The proposed solution is a method in which, during the contacting step, the mutants are transferred from the bank into serum.

3.4 However, this solution cannot be considered to involve an inventive step, for the following reasons: It is well known to persons skilled in the art that the mechanisms of meningococcal meningitis include an extracellular growth stage that takes place in blood (i.e. a serum growth stage), as indicated in D3 (page 223, column 2, paragraph I.).

3.4.1 Consequently, a person skilled in the art aware of the method described in D2 (which further indicates that mutagenesis studies carried out on the molecular mechanisms of meningococcal meningitis are

desirable (page 5397, column 1, lines 42-46)), and aware from D3 that the serum growth capacity is one of the essential mechanisms of *N. meningitidis* infection, would consider it obvious, when seeking a solution to the stated problem, to modify the method of D2 with a view to exposing the mutants to an environment consisting of serum in order to select mutants that have a reduced serum growth capacity, and would thus arrive at a method as per claim 2.

3.5 In light of the above, the present application fails to comply with the requirements of PCT Article 33(3), since the subject matter of claims 1 to 3 does not involve an inventive step.

4. INDUSTRIAL APPLICABILITY (PCT Article 33(4))

4.1 The subject matter of claims 1 to 3 is industrially applicable (PCT Article 33(4)).